

Risk factors for outcomes were analyzed and included Hematopoietic cell transplantation co morbidity index (HCT-CI) score (Sorró, Blood 2005), relapse risk score (Kahl, Blood 2007) and risk stratification by age groups. 110 patients (69%) had low or standard relapse risk score while 49 (31%) had high score. 26 patients (16%) had HCT-CI score of 0, 48 patients (30%) had score of 1-2, 48(30%) had score of 3-4 and 32 (20%) had score of 5 or above.

Increasing HCT-CI score had a significant impact on OS in both univariate and multivariate analysis ( $p < 0.05$ ). HCT-CI of 1-2, 3-4 and 5 plus was prognostic for OS (HR 2.6, 2.9 and 3.6;  $p = 0.006$ , 0.005 and 0.001 respectively). For PFS, high relapse risk score was prognostic (HR 7.8,  $p = 0.001$ ) but increasing HCT-CI score lost significance. Risk stratification by age groups (60-65, 66-70 and 70 plus) did not show any prognostic implication on either PFS or OS.

Our results support the use of RIC HCT as a potentially curative treatment modality for elderly patients, and as well support the prognostic value of HCT-CI score. Elderly patients with high scores ( $> 5$ ) may not benefit from undergoing HCT even with RIC or NM HCT.

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#### BLAST PERCENTAGE PRIOR TO TRANSPLANTATION IS THE STRONGEST PREDICTIVE FACTOR FOR SURVIVAL AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) IN PATIENTS WITH MYELODYSPLASTIC SYNDROME (MDS)

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**Background:** Allogeneic hematopoietic stem-cell transplantation (HSCT) is the only curative treatment for patients (pts) with myelodysplastic syndromes (MDS) or secondary acute myeloid leukemia (sAML) with long-term survival rates between 25% and 70%. Disease stage at time of transplantation has been strongly correlated with transplant outcomes; current data suggests that achieving a low pre-transplant tumor burden is critical for a successful allograft. We sought to retrospectively identify the relationship between pre-transplant blast percentage and clinical outcomes following HSCT in MDS pts. **Methods:** We conducted a retrospective review of pts with MDS who received an allogeneic HSCT in our institution from 1998 to 2010. We previously reported the impact of clinical characteristics and treatment on outcomes in this patient population. We quantified the pre-transplant marrow burden on all pts with available pathology. Bone marrow biopsy was performed prior to allogeneic HSCT and pts' blast burden was quantified as low or high on the basis of blast percentage ( $< 5\%$  or  $\geq 5\%$  respectively).

**Results:** 35 MDS pts were transplanted at our institution between 1998 and 2010. Median age was 51 years (range: 24-66); male to female ratio 1:1; matched related donor 46% ( $n = 16$ ); matched unrelated donor 54% ( $n = 19$ ). Cytogenetic risk group by IPSS: good, 40% ( $n = 14$ ), intermediate, 37% ( $n = 13$ ), poor, 23% ( $n = 8$ ). Graft source was mobilized peripheral blood in 80% ( $n = 28$ ) and bone marrow in 20% of pts ( $n = 7$ ). Information on marrow blast percentage prior to transplant was available for 32 pts; survival was 53% at 1 year and 40% at 2 years in this group. Survival at one year was superior for pts with low blast burden compared to those with  $\geq 5\%$  blasts (68% vs. 30%, respectively;  $p = 0.036$ ). Among the 17 pts alive at 1 year, 77% had low blast burden (vs. only 40% in those pts who didn't survive past day +365). Blast percentage prior to transplant also predicted for survival on multivariate analysis ( $p = 0.042$ ).

**Conclusions:** Our retrospective analysis identified blast percentage as an independent predictor of clinical outcomes in MDS pts undergoing HSCT. Our results are consistent with the current literature. Prospective evaluation of multiple clinical variables in a larger patient population is warranted to better characterize prognostic factors. The role of cytoreductive therapy prior to transplant in order to achieve a low blast burden should be further evaluated in this setting.

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#### THE EFFECT OF KIRS EXPRESSION PROFILE IN DONOR/RECIPIENT PAIRS IN HLA IDENTICAL SIBLING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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**Objective:** We investigated the distribution characteristics of KIRs expression profile in donor/recipient pairs with acute leukemia (AL) receiving HLA-identical sibling hematopoietic stem cell transplantation (sib-HSCT). We further explored the effect of KIRs expression profile in donor/recipient pairs on clinical outcome.

**Methods:** The genotypes of donor/recipient KIRs were determined by polymerase chain reaction- sequence specific primer (PCR-SSP) for 80 pairs of donor/recipient receiving HLA-identical sibling hematopoietic stem cell transplantation.

**Results:** 1. In 80 pairs of donor/recipient: (i) the KIRs were completely identical in 57.5% of donor/recipient pairs; (ii) the donors' KIRs contained the recipients' in 13.75% pairs; (iii) the recipients' KIRs contained the donors' in 17.5% of pairs; (iv) the KIRs were completely different in 11.25% pairs. The graft versus host (GVH) direction KIR-matched group was 75%. The percentage of group donor B/X and group donor A/A was 50%, respectively. 2. Comparing the patients from GVH direction KIR-matched and mismatched group, the incidence of acute (a) GVHD was 60% and 30%, respectively ( $p = 0.0222$ ), and 2-year OS was 62.96% and 94.12%, respectively ( $p = 0.0492$ ). Particularly, grade III-IV aGVHD rate of KIR-matched group was higher than that of non-KIR matched group (15% vs 0%). 3. Donor B/X group had a higher 2-year OS and 2-year relapse-free survival (RFS) compared with donor A/A group (89.23% vs 49.57%,  $p = 0.0159$ , and 90% vs 59.71%,  $p = 0.0239$ , respectively). Patients with three or less aKIRs had a lower 2-year OS (58.9% vs 92.44%,  $p = 0.0338$ ) and a lower RFS (65.14% vs 92.59%,  $p = 0.0398$ ), compared with patients with more aKIR.

**Conclusions:** Donor KIR genotype appears to have a direct impact on aGVHD, OS and RFS. Therefore, donor KIR genotype should be evaluated as an outcome predictor of the HLA-identical sib-HSCT.

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#### COMPARABLE SURVIVAL AFTER UNRELATED AND RELATED ALLOGENEIC STEM CELL TRANSPLANTATION PERFORMED AT COMMUNITY CANCER CENTERS

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The outcomes after unrelated donor hematopoietic stem cell transplantation (MUD HCT) have improved over the past decade with survival equivalent to related donors (RD) HCT. Although MUD HCT is becoming more available in community cancer centers, there is very limited literature available about the outcomes of MUD HCT outside the academic setting. To study the above question, we performed a retrospective analysis of the outcomes of 56 consecutive patients that underwent HCT (30 MUD, 26 RD) between August 2007 and July 2010 at our community cancer center. All patients had a minimum follow up of one year post HCT. There was no statistical difference between MUD and RD recipients (Table 1). Conditioning regimens used were Fludarabine/Melphalan in 13 patients (3 MUD & 10 RD), Busulfan based in 28 patients (19 MUD & 9 RD), Fludarabine/TBI in 10 patients (5 MUD & 5 RD), Cytosan/TBI in 2 patients (1 MUD & 1 RD) and other in 3 patients (2 MUD & 1 RD). Graft versus Host Disease (GVHD) prophylaxis regimens used were Tacrolimus/Methotrexate in FIC HCT recipients and Cyclosporine/Mycophenolate mofetil in RIC/NMA HCT recipients. MUD HCT recipients received additional Thymoglobulin (4.5 mg/Kg). Median time to neutrophils engraftment was 14 days for RD and 13 days for MUD. The cumulative incidence of acute GVHD (grade I-IV) was 60% for MUD and 54% for RD. The cumulative incidence of chronic GVHD was comparable between both groups of 63% and 72% for MUD and RD respectively.

With median duration follow up of 2 years, there was no statistical difference in overall survival (OS) at one and 2 years of 57% and 40% for MUD recipients versus 65% and 54% for RD recipients respectively ( $p = 0.48$ ). Similarly, disease free survival (DFS) at 1 and 2 years was 50% and 36% versus 50% and 22% for MUD and RD recipients respectively ( $p = 0.24$ ). There were more relapses in RD recipients with cumulative incidence of 34% and 59% at 1 and 2 years respectively compared to 23% at 1 and 2 years in MUD recipients. Non relapse mortality (NRM) at day 100 was 10% and 8% for

MUD and RD recipients; respectively. MUD recipients had a higher cumulative incidence of non-relapse mortality at 2 years of 34% compared to 19% for RD recipients.

**Conclusions:** Outcomes after MUD HCT when performed at community cancer centers were not inferior to outcomes after RD HCT. It seems feasible to perform MUD HCT at community cancer centers with outcomes comparable to published literature.

	Mud (%)	RD (%)	p
Number	30	26	
Median Age (Range)	55.86 (23-71)	53.8 (35-73)	0.18
Gender (F/M), %	(10/30), 33.3%	(13/26), 50%	0.32
Median CD 34 cell dose (Range)	7.18 (1.89-11.35)	7.04 (2.87-10.4)	0.16
Diagnosis (Acute leukemia Vs Others)			0.83
ALL	2 (7%)	7 (27%)	
AML/MDS	19 (63%)	11 (42%)	
Multiple Myeloma	0	3 (11%)	
CLL/T-PLL	1/1 (7%)	1/1 (8%)	
HD/NHL	1/2 (10%)	1/1 (8%)	
MF	1 (3%)	1 (4%)	
SAA	2 (7%)	0	
CML	1 (3%)	0	
Status at Transplant			0.21
CR1	13 (43%)	7 (27%)	
CR2 or beyond	6 (20%)	3 (11.5%)	
PR	2 (7%)	3 (11.5%)	
Persistent/Progressive Disease	6/2 (27%)	5/5 (38.5%)	
Primary Refractory	1 (3%)	3 (11.5%)	
Cytogenetics			0.86
Normal Cytogenetics	12 (40%)	12 (46%)	
High Risk Cytogenetics	18 (60%)	14 (54%)	
Prior Transplant			
Autologous	1	5	
Allogeneic	2	1	
Co-Morbidity Index			0.84
CCI 1-2	10 (33%)	8 (31%)	
CCI 3 or more	20 (67%)	18 (69%)	
Distance From Transplant Center			0.43
Median	21.2 miles	23.1 miles	
Range	5-131 miles	4.9-130 miles	
Conditioning Regimens			0.39
RIC/NMA	15 (50%)	17 (65%)	
FIC	15 (50%)	9 (35%)	

MF indicates myelofibrosis; RIC, reduced intensity conditioning; FIC, full intensity conditioning; NMA, non-myeloablative.

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#### HAPLOIDENTICAL TRANSPLANT WITH HIGH DOSE OF UNMANIPULATED CD34, IN VIVO T CELL DEPLETION WITH ALEMTUZUMAB AND RIC REGIMEN. GOOD ENGRAFTMENT RATE, LOW GVHD INCIDENCE AND ENCOURAGING SURVIVAL. SINGLE CENTER EXPERIENCE IN COLOMBIA

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For a successful haploidentical transplant is necessary to overcome the HLA barrier. We present our experience using high dose of unmanipulated CD34, in vivo T cell depletion and a RIC regimen.

After a signed informed consent seventeen patients received 20 transplants (3 ptes. underwent a second haplo transplant after engraftment failure of the first). 9 were women, median age was 17.3 years (7-36), 40% were under sixteen. 5 patients had high risk AML CR1 or CR 2; 3 had high risk ALL CR1 or CR3; 5 heavily transfused Fanconi anemia, 1 aplastic anemia, 1 myelofibrosis, 1 dendritic cell leukemia CR2, 1 hemophagocytic lymphohistiocytosis.

Two patients received the haplo transplant after an unsuccessful cord blood transplant. The donors were 16 mothers, 3 siblings and 1 father. 80% had 3 out of 6 match.

The conditioning was cyclophosphamide 2000 mgs/m<sup>2</sup>, fludarabine 120 mgs/m<sup>2</sup> +/- thiotepa 5 mgs/kg. In 11 procedures TBI 200-400 Cgy was added. In vivo T cell depletion was done with Alemtuzumab 0.2 mg/kg/day from day -4 to zero. All patients received unmanipulated peripheral blood CD34 obtained by apheresis (median 12 mill/kg) in 2 cases bone marrow was added. The GVHD prophylaxis was accomplished with CyA for 180 days and MMF for 30. Filgrastim was administered from D+6 until neutrophil recovery.

Neutrophil engraftment occurred at median of 11 days (9-14) in 82% of the patients after first transplant and in 100% after the second, 1 patient had a secondary graft failure. The incidence of acute GVHD GI-II was 25%, there were no cases of GIII-IV. One patient had aGVHD GIII after DLI, chronic GVHD was presented in 40% of the patients, in all cases limited, and in 50% of them treated with only topical medication.

The 100 days mortality was 17.64 % and with a median follow up of 16 months (1-38) the overall survival was 53.5%.

**Conclusion:** The strategy of use high dose of unmanipulated CD34, in vivo T cell depletion and a RIC preparative regimen produce a reliable engraftment, low incidence of GVHD, low day 100 mortality and good overall survival in this high risk group. It deserves more studies.

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#### EARLY HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ALL PATIENTS AFTER REDUCED INDUCTION CHEMOTHERAPY

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Hematopoietic stem cell transplantation (HSCT) is only curable treatment in ALL patients. However, the efficacy of induction, consolidation chemotherapy and early hematopoietic stem cell transplantation remain unclear.

Therefore, at our center, patients with newly diagnosed ALL, are randomly divided into 2 arms from 2008 to 2011. Patients in the study arm received reduced induction chemotherapy (vincristine 1 mg/m<sup>2</sup> every week for 4 weeks plus dexamethasone 24mg/d for 28 days) and undergone early HSCT after disease stabilized within 15-30 days without intention of achieving complete remission (CR). The control arm received conventional chemotherapy followed by HSCT. Both arms received busulfan (4mg/kg for 4 days) plus cyclophosphamide (60mg/kg for 2 days) as a conditioning regimen. Here, we compare the efficacy of these two kinds of treatment.

A total of 90 patients enrolled in the study. Eighteen patients allocated to the study arm and 72 others allocated to the control arm. The median age was 21.5 years (range: 16-33) in the study arm and 22 years (range: 3-49) in the control arm. All patients underwent Allogeneic HSCT with peripheral blood source. The median waiting time from diagnosis to HSCT was 217 days (range: 45-708) in the control arm. In the study arm, 14 patients (78%) were in CR1. The median follow-up time was 15.5 months (range: 2-32) in the study arm and 12.5 months (range: 1-39) in the control arm. Relapse occurred in 2 (11.1%) and 6 (8.3%) patients of the study and the control arms, respectively. Five patients (27.7%) of the study arm and 10 patients (13.5%) of the control arm were died. The causes of death were GVHD and sepsis in 3 (60%) patients and relapse in 2 (40%) patient in the study arm. The causes of death were GVHD in 6 (60%) patients and relapse in 4 (40%) patients in the control arm. One-year overall survival was 81.9% (SE: 9.5%) and 84.8% (SE: 4.8%) in study and control arms, respectively (p = 0.221). One-year disease-free survival was 81.9% (SE: 9.5%) and 82.4% (SE: 4.9%) in study and control group, respectively (p = 0.532).

Reduced induction followed by early transplantation without consolidation reveals no significant statistical different outcome compared with routine treatment. This result might be due to small size of patients and short time of follow-up. A study with more cases and long time follow-up is recommended.